

1 **MULTIPLE DRUG DELIVERY SYSTEM & METHOD**

2 Background of the Invention

3 (1) Field of the Invention

4 The present invention relates generally to pharmacology and, more particularly, to
5 smoking cessation methods and aids.

6 (2) Description of the Prior Art

7 Cigarette smoking has been associated with lung cancer, heart disease, and other
8 ailments, including birth defects. Unfortunately, addiction to cigarette smoking is
9 difficult to break because the user has both a chemical addiction to the nicotine delivered
10 via the cigarette and a psychological addiction to the hand to mouth motion. In addition,
11 the nicotine levels delivered via a cigarette are not constant, but rather are delivered as
12 multiple spiking doses. The most successful solution to break cigarette use will then be
13 one that emulates most closely the delivery of nicotine, both chemically and
14 mechanically, by a cigarette.

15 Studies have shown that smokers using nicotine gum, patch, nasal spray, inhaled
16 nicotine, or nicotine sublingual tablets are about 1.5 to 2 times more likely to stop
17 smoking than smokers using no cessation aid, and evidence suggests that bupropion may
18 be even more effective (see, Silagy et al., Cochrane Database Syst. Rev., No. 2,
19 p.CD000146 (2000)). However, each of the existing smoking cessation aids has
20 drawbacks, and none has proven fully effective. Additionally, resolution of nicotine
21 addiction requires that the addict gradually reduce the dosage over time. Prior art
22 embodiments have accomplished this by providing devices at different doses of nicotine,
23 such that the user can switch to devices with progressively lower dose over time.

1 Cigarette smoking involves a hand-to-mouth ritual that may be repeated over
2 70,000 times per year. Since smoking cessation requires giving up a highly ingrained
3 habitual motion as well as giving up nicotine, an effective smoking cessation aid should
4 address the behavioral components of smoking as well as providing nicotine replacement
5 therapy. A smoking cessation aid should give the smoker the comfort of an oral and
6 tactile ritual, while at the same time supplying nicotine. However, a smoking cessation
7 device that is too similar to a conventional cigarette and provides oral sensations and
8 tactile stimuli that too closely mimic tobacco smoking may not be ideal. A smoker using
9 such a device might find it too easy to relapse into cigarette smoking (see, e.g., Schneider
10 et al., *Addiction*, 91:1293-1306 (1996)). Thus, a smoking cessation aid that provides the
11 synergistic combination of nicotine plus oral and tactile stimuli, while not too closely
12 approximating a conventional tobacco cigarette, seems most desirable.

13 Various smoking cessation aids have been developed, including nicotine gum
14 (see, e.g., U.S. Pat. No. 3,845,217); nicotine transdermal patch (see, e.g., U.S. Pat. No.
15 4,915,950); nicotine nasal spray (see, e.g., AU 664 41); nicotine inhaler (see, e.g., U.S.
16 Pat. Nos. 4,920,989 and 4,953,572); and sustained-release bupropion hydrochloride (see,
17 e.g., Jorenby et al., *N. Engl. J. Med.*, 340:685-91(1999)). Other examples of smoking
18 cessation aids include nicotine nose drops (see, e.g., U.S. Pat. No. 4,579,858); nicotine
19 lozenges (see, e.g., U.S. Pat. Nos. 4,806,35 and 5,549,906); smoke-free cigarettes (see,
20 e.g., U.S. Pat. Nos. 4,284,089, 4,676,259, 4,736,755, 4,813,437, 5,284,163, and
21 6,041,789); compositions comprising nicotine metabolites (see, e.g. U.S. Pat. No.
22 5,869,505); and drinkable nicotine solutions (see, e.g., WO 99/55371).

1 Certain devices developed to facilitate smoking cessation provide the nicotine and
2 oral stimulation, but no repetitive hand-to-mouth motion is required to use these aids.
3 These aids include chewing gums, tablets and lozenges.

4 Chewing gum was an early carrier employed to deliver nicotine or other drugs.
5 United States Patent 4,276,890 issued to Fichera July 7, 1981 describes the use of
6 chewing gum for the delivery of a chemical to aid in the cessation of smoking. United
7 States Patent 4,753,800 issued to Mozda June 28, 1988 describes the use of chewing gum
8 to deliver nicotine and other drugs, but not specifically for the purpose of aiding in the
9 cessation of smoking.

10 Tablets and lozenges are another embodiment of a drug delivery device applied to
11 smoking cessation. US Patent No. 6248760 issued 06/19/2001 to Wilhelmsen for Tablet
12 Giving Rapid Release of Nicotine for Transmucosal Administration teaches a tablet
13 embodiment. US Patent No. 6280761 issued 08/28/2001 to Santus for Nicotine lozenge
14 teaches the use of a lozenge for delivery of nicotine.

15 Aids that provide nicotine, oral stimulation, and repetitive hand-to-mouth motion
16 for use include suckers or lollipops and an inhalation tube. US Patent No. 5058544
17 issued 09/17/1991 to Mascarelli, et al. for Cigarette Substitute provides an edible portion
18 having a small amount of a nicotine composition sufficient to satisfy the desires of the
19 cigarette smoker. Preferably, the edible portion would be shaped in the form of a
20 conventional lollypop, which would preferably have a hard semi-hard candy.

21 PUBLICATION US20020059939 for Device and method for the cessation of
22 smoking teaches an oral device providing a tubular chamber used to intake liquid/gas and
23 the delivery of nicotine for the cessation of smoking.

1 These prior art devices do not teach the incorporation of a step-down dosage level
2 regimen within a device that satisfies the hand-to-mouth behavior and oral stimulation. A
3 step-down regimen with only single dosage level devices require the user to abandon the
4 current dosage level and abruptly move to the next lower level. This can cause the
5 recrudescence of withdrawal symptoms.

6 Devices with a plurality of doses have been described. US Patent No. 6358060
7 issued 03/19/2002 to Pinney et al. for Two-stage transmucosal medicine delivery system
8 for symptom relief describes a delivery system provided in chewing gum form or lozenge
9 form and provides an initial dose of medicine capable of achieving a rapid
10 pharmacological effect and a second dose of medicine for a prolonged effect. US Patent
11 No. 6344222 issued 02/5/2002 to Cherukuri, et al. for Medicated chewing gum delivery
12 system for nicotine teaches a chewing gum delivery system that has nicotine, a gum base
13 and a buffer system with an improved release rate for the nicotine. The delivery system is
14 capable of delivering initial and second doses of a craving reduction active or other
15 actives (e.g., nicotine), the combination of which rapidly reduces cravings, or provides
16 some other pharmacological effect, and provides the pharmacological effect or protection
17 from such cravings over a prolonged period of time beyond the initial dose. These prior
18 art devices, while incorporating multiple doses within a device, do not satisfy the hand-
19 to-mouth motion.

20 Each of these prior art embodiments has drawbacks associated with them.
21 Nicotine patches may irritate the skin, and some smokers are dissatisfied with the lack of
22 rapid nicotine absorption from the patch. Nicotine nasal sprays may irritate the nose and
23 throat. More importantly, none of these smoking cessation aids simulates the tactile

1 sensations or hand-to-mouth behaviors that form an integral part of the smoker's
2 addiction. Patches provide no oral or tactile stimulus; gum, lozenges, and drinkable
3 solutions stimulate only the mouth, and nasal sprays stimulate only the airways. These
4 aids lack the important synergistic combination of nicotine, oral stimulation, variable
5 dose, and hand-to-mouth behaviors that smokers' desire. Although the inhalation tube
6 and lollipop do satisfy these needs, these prior art devices do not teach the incorporation
7 of a step-down dosage level regimen within a single device. A step-down regimen with
8 only single dosage level devices require the user to abandon the current dosage level and
9 abruptly move to the next lower level. This abrupt change in dosage can cause
10 withdrawal symptoms. Prior art single-dose lollipop embodiments, while satisfying the
11 chemical and psychological dependencies, lack the dosage step-down that appears
12 necessary for users to progress to lower dosages and eventual resolution of the addiction.

13 Therefore, a need exists for a smoking cessation aid that combines the nicotine,
14 oral stimulation, variable dose, and hand-to-mouth behaviors that smokers desire, and
15 provides a series of multiple-dose devices with overlapping doses such that an addict can
16 move to progressively lower doses without abrupt lowering the dose.

17 Summary of the Invention

18 The present invention is directed to a multiple-dosage level device that provides
19 nicotine or nicotine equivalent, variable dose, repetitive hand-to-mouth motion, and oral
20 stimulation to aid in the cessation of smoking.

21 Accordingly, one aspect of the present invention is to provide a device for the
22 cessation of an addiction, including a lollipop with hard candy exterior and chewable
23 core, wherein exterior has a first dose level and core has a second dose level.

1 Another aspect of the present invention is to provide a device for the induction of
2 tachyphylaxis, comprising: A lollipop with hard candy exterior and chewable core,
3 wherein exterior has a first dose level and core has a second dose level.

4 Another aspect of the present invention is to provide a method for cessation of
5 chemical addiction, comprising: providing a series of multiple-dosage devices, wherein
6 each device has at least 2 doses, the first available dose being higher than the next
7 available dose, and each successive device in the series has the first available dose at the
8 about same concentration as the second available dose of the prior device in the series.

9 Still another aspect of the present invention is to provide a method for the
10 induction of tachyphylaxis, comprising: providing a series of multiple-dosage devices,
11 wherein each device has at least 2 doses, the first available dose being lower than the next
12 available dose, and each successive device in the series has the first available dose at the
13 about same concentration as the second available dose of the prior device in the series.

14 These and other aspects of the present invention will become apparent to those
15 skilled in the art after a reading of the following description of the preferred embodiment
16 when considered with the drawings.

17 Brief Description of the Drawings

18 Figure 1 is a cross-sectional view of a lollipop constructed according to the present
19 invention.

20 Detailed Description of the Preferred Embodiments

21 In the following description, like reference characters designate like or
22 corresponding parts throughout the several views. Also in the following description, it is
23 to be understood that such terms as "forward," "rearward," "front," "back," "right,"

1 “left,” “upwardly,” “downwardly,” and the like are words of convenience and are not to
2 be construed as limiting terms.

3 Referring now to the drawings in general, the illustrations are for the purpose of
4 describing a preferred embodiment of the invention and are not intended to limit the
5 invention thereto. As best seen in Figure 1, the device is configured as a lollipop,
6 generally referenced as 10, having an edible portion 11 and a support 12. The edible
7 portion is comprised of a hard candy shell 15 and a gum interior 20. The hard candy
8 shell can be of a variety of shapes, including cylindrical, spherical, orthogonal, and the
9 like, without departing from the invention. The dimensions of the lollipop are such that
10 the lollipop will feel comfortable in the user's mouth, generally the same diameter or
11 cross-section as currently available hard candies or lozenges. The support 12 is of a
12 dimension that satisfies the user's tactile needs. By way of example, it may be equivalent
13 to a typical lollipop stick, or may be larger, such as the dimensions of a cigarette.

14 The lollipop contains a pharmaceutical chemical having at least two dose levels, a
15 first dose level in the candy shell and a second dose level in the gum interior. In the case
16 of a device for the resolution of cigarette addiction, the chemical is nicotine, including
17 nicotine derivatives, at doses ranging from high doses designed to satisfy heavy nicotine-
18 intakers to a low dose of no nicotine.

19 In the cases of devices to break addiction, the doses would start with the higher
20 dose externally and progress to lower doses internally. A range of devices with close or
21 overlapping dosages would be provided.

22 A multiple-dosage level device provides gradual step-down, allowing the user to
23 progress from a higher dose to a lower dose within the same device. The immediate

1 chemical craving would be satisfied by the higher, first dose. Over time, the user would
2 become habituated to the second, lower dose, such that when the user moved to the next
3 lower dosage device, in which the first dose is the same concentration as the second dose
4 of the previous level, the user would be accustomed to the initial dosage level.

5 Use of a lollipop that incorporates nicotine in such a step-down dose would also
6 satisfy the psychological or habitual addictions associated with cigarette smoking.

7 More than 2 levels of a chemical may also be provided, for example by stratifying
8 the candy shell or incorporating the multi-level chewing gums as described in the prior
9 art US Patents No. 6358060 and 6344222 and incorporated herein by reference in their
10 entirety.

11 The present invention provides a controlled release of predetermined levels of a
12 pharmaceutical over time. By stratifying the hard candy shell into different layers, and
13 alternating the levels of a drug, spiking dosages can be delivered. Alternatively, the drug
14 itself can be varied between strata, thereby delivering combinations of drugs. More
15 specifically, a first drug can be delivered in a stratum and a second drug can be delivered
16 in the next-most interior stratum. The drug can be a pharmaceutical agent or a non-
17 pharmaceutical agent, including sweeteners such as sugar, corn syrup, aspartame,
18 saccharin, and the like.

19 Other benefits of the present invention include increased compliance by otherwise
20 recalcitrant users, such as children and mental patients. The present invention would be
21 of great use in mental patients, or other persons without the capacity to endure the slight
22 discomfort associated with abrupt changes in medication. Compliance would be higher in
23 these persons if using the present invention than if using prior art embodiments. The

1 device would be especially effective when sequentially administering multiple drugs to
2 these users. In these embodiments, the internal core need not necessarily be chewable
3 gum, but can be any candy, including hard candy, taffy, caramel, and the like. The nature
4 of the internal core can be modified to satisfy the requirements of the specific application.

5 A specific example embodiment, not intended as a limitation, is the use of the
6 device for the administration of cancer chemotherapeutic drugs to young children.
7 Certain chemotherapeutics induce nausea, and therefore an anti-nausea drug is frequently
8 administered prior to administration of the chemotherapeutic to reduce the nausea. In the
9 specific embodiment, an anti-nausea drug can be incorporated in the exterior shell, and
10 the chemotherapeutic drug into the internal chewable core. In this application, a child
11 would received the anti-nausea agent while eating the exterior shell, preferably slowly
12 enough for the drug to be in effect when the child started chewing the chewable core and
13 started receiving the chemotherapeutic drug. The chewable core need not necessarily be
14 chewing gum, but can be any chewable candy or substance, such as taffy, caramel, and
15 the like.

16 The present invention includes a device for drug delivery, including at least 2
17 different juxtaposed layers of edible matter, each layer having a dosage level of
18 medication and the layers alternate dosage level. The at least two different juxtapose
19 layers of edible matter may be more than two layers of edible matter and the layers have
20 variable dosage levels.

21 Variable dosage levels results in spiking delivery of the drug. Alternating or
22 varying delivery permits the user to maintain the device in his/her mouth, yet have
23 variable levels of drug delivery. This variable delivery more closely mimics actual

1 cigarette smoking, and can break the hand-to-mouth motion or habit because the user can
2 gradually reduce manipulation of the device, while receiving variable doses of the drug.

3 Thus using the present invention in an embodiment that uses a drug that satisfies
4 nicotine addiction provided with alternating doses closely mimic a smoker's nicotine
5 uptake when smoking a cigarette. To further emulate smoking, the device can further
6 include a support device for hand-control or manipulation of the device. This support
7 permits removing the device from the mouth, for example if the user needs to adjust the
8 intake of the drug. The support device can be a normal candy support, such as a lollipop
9 stick, or may be larger than a normal candy support device, in order to satisfies a cigarette
10 user's tactile needs

11 A device according to the present invention also preferably has a chewable core,
12 wherein the core has at least one dose level of the drug. The chewable core can be a
13 chewable candy, such as gum, taffy, caramel, and the like.

14 In one embodiment, the outer-layer drug is an anti-side-effect drug directed
15 toward alleviating side-effects of an inner-layer drug. For example, if the inner-layer
16 drug is a chemotherapeutic drug that causes nausea, the outer-layer drug can be an anti-
17 nausea agent.

18 A method for using the device to deliver a drug includes providing a device with
19 multiple doses. A series of devices can also be provided, wherein the dosage levels are
20 staged between devices, providing an incremental change of dosage levels, wherein the
21 incremental levels progress from low dosage to high dosage, high dosage to low dosage,
22 and combinations thereof. For example, a drug that causes severe side effects and is
23 otherwise useless may be useful if the body can adapt to the side-effects. Such an

1 adaptation can potentially be achieved by incrementally increasing the dose levels from a
2 very low starting dose. After the curative effective is achieved, the drug administration
3 can be stopped, for the dosage can be tapered down to prevent withdrawal symptoms. In
4 the case of a chemical addiction, a method for resolving the addiction includes providing
5 a device according to the present invention having at least 2 dosage levels of an addictive
6 drug substitute. For greater efficacy, a series of multiple-dosage devices can be provided,
7 wherein each device has at least 2 doses, the first available dose being higher than the
8 next available dose, and each successive device in the series has the first available dose at
9 the about same concentration as the core in the prior device in the series. Thus, a series
10 of multiple-dosage devices would have high (H) and low (L) drug dosage levels: H₁L₁,
11 H₂L₂, H₃L₃, H₄L₄, H_nL_n, H_{n+1}L_{n+1}, H_{n+2}L_{n+2}. H_{n+2} can be similar to, less than, or
12 higher than L_{n+1}. H_{n+2} can be higher than L_{n+1} such that the user feels satisfied by the
13 slightly higher dose of H_{n+2} than by the low dose of L_{n+1}.

14 In the case of chemical addiction to nicotine, the devices would contain nicotine
15 or a nicotine substitute. The nicotine addiction can be from the nicotine inhaled from
16 smoking tobacco, such as from cigarettes, pipes or cigars, or from oral tobacco products,
17 such as chewing tobacco, snuff, and the like.

18 A preferred embodiment of the present invention is a device for the administration
19 of a drug. The device includes an edible drug delivery device with a flavored exterior
20 and a chewable core. The drug in the flavored exterior and core can be the same,
21 similar, or different drugs. The device can be used to deliver a drug for the purposes of
22 medical treatment, or for the purposes of stopping a chemical addiction.

23 For example, the drug in the flavored exterior can be at least one anti-side-effect

1 agent directed towards alleviating the effects of the drug in the at least one inner layer.
2 For example, the inner drug may be a chemotherapeutic agent that causes nausea, and the
3 otherefore the outer layer drug is an anti-nausea drug.

4 The flavored exterior can be a hard candy. The drug may be stratified in the hard
5 candy shell into different layers, and the levels of the drug are alternated in the different
6 layers, resulting in delivery of variable or spiking dosages to the user.

7 The core has at least one drug, which can be a second dose level. For example,
8 the chewable core for a device directed towards cessation of nicotine addiction contains
9 nicotine or nicotine substitutes at a second dose level. The core can be a chewable candy,
10 such as gum, taffy, caramel, and the like.

11 The device may also include a support, such as a typical lollipop stick, or may be
12 larger, such as the dimensions of a cigarette or cigar.

13 The device can be directed toward the cessation of a chemical addiction,
14 including nicotine addiction, such as from smoking or chewing tobacco products. In the
15 embodiment for the cessation of nicotine addiction, the flavored exterior contains
16 nicotine at a first dose level and the chewable core contains nicotine at a second level.
17 The nicotine is preferably stratified in the hard candy shell into different layers, and the
18 levels of the drug are alternated, resulting in delivery of spiking dosages. The device for
19 the cessation of smoking preferably includes a support, such as a typical lollipop stick, or
20 may be larger, such as the dimensions of a cigarette or cigar, such that manipulation of
21 the support satisfies the user's tactile needs.

22 Certain modifications and improvements will occur to those skilled in the art upon
23 a reading of the foregoing description. By way of example, as an alternative to the

1 foregoing description of preferred embodiments, the device can be used to induce
2 tachyphylaxis, that is, a decreased response to a drug given over a period of time so that
3 larger doses are required to produce the same response, in cases where tachyphylaxis is
4 desired. Induction of tachyphylaxis can be used, for example, to protect against
5 accidental overdoses, or in homeopathy to stimulate a patient's weakened response. By
6 using a system of multiple-dosage, overlapping-dose devices, tachyphylaxis can be
7 induced while minimizing the effects of increasing dosage.